Urticaria and Angioedema

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Conf univ

Urticaria (Hives)

- transient
- self-limiting
- erythematous swelling of the skin (epidermis and superficial dermis)
- associated with itching,
- which usually resolves within 24 hours

Angioedema

- First described by Quincke in 1882
- Well-demarcated non-pitting edema
- Reaction occurs deeper in dermis and subcutaneous tissues
- Often caused by same pathological factors that cause urticaria
- Face, tongue, lips, eyelids most commonly affected
- May cause life-threatening respiratory distress

Classification (1)

- According to evolution:
  - Acute urticaria (< 6 weeks)
  - Chronic urticaria (> 6 weeks)

Classification (2)

- According to provoking factors:
  - Spontaneous urticaria
  - Physical urticaria (**Cold** contact urticaria, **Heat** contact urticaria, **Pressure** urticaria, **Solar** urticaria, **Dermographic** urticaria, **Vibratory** urticaria)
  - Other urticaria types (**Aquagenic** urticaria, **Cholinergic** urticaria (by increase of body core temperature due to physical exercises, spicy food), **Contact** urticaria (by urticariogenic substance), **Exercise induced** urticaria)

Classification (3)

- According to the patogenetic mechanism:
  - Urticaria / angioedema due to **hypersensitivity reactions** IgE mediated (drugs, food, insect venoms)
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  - Urticaria / angioedema due to **pseudoallergic reactions** (IgE independent mechanisms – NSAIDs, opioids, vancomycin, contrast dye)
- Urticaria / angioedema due to **toxic reactions** (food contaminated with bacteria that produce histamine – some species of fish)
- Urticaria / angioedema due to **immune complexes** (serum sickness, viral infections, postransfusion, due to thyroid pathology, paraneoplastic syndrome etc.)

Classification (4)

Diseases related to urticaria for historical reasons:

- Urticaria pigmentosa (mastocytosis)
- Urticarial vasculitis
- Familial cold urticaria (vasculitis)
- Nonhistaminergic angioedema (e.g. HAE)

Etiology

Triggers of acute urticaria:

- IgE-mediated allergic urticarial reactions are triggered by:

- **drugs** (penicillin, sulfa drugs, antibiotics, and contrast dye),
- **foods** (shellfish, salicylates in berries, tomatoes, yeast, and penicillin in blue cheese, **nuts** (especially peanuts), **food additives** (sodium benzoate),
- **insect bites** (mosquitoes, bees, wasps, scabies, or animal mites).

- Nonimmunologic mediators of urticaria include:

- aspirin and opiates,
- physical agents that work through the prostaglandin pathway or degranulate mast cells.

Etiology

- **Causes of chronic urticaria:**

- **occult infections** (sinusitis, gallbladder disease, *Helicobacter pylori,* yeast infections, tooth abscesses, or silent hepatitis),
- **collagen diseases**
- **tumors**, especially Hodgkin's lymphoma.

- **Autoimmune disorders**

Pathogenesis

- Mast cells, the primary effector cells in urticaria/angioedema, are found in high numbers throughout the body and particularly within the subcutaneous tissue.
- After activation of mast cells there is a rapid release (<10 minutes) of histamine, leukotriene C_4 (LTC_4), and prostaglandin D_2 (PGD_2) leading to **vasodilation,** subcutaneous and intradermal **leakage of plasma** from postcapillary venules, and **pruritus**.
- In addition, there is a more delayed (4 to 8 hours) production and secretion of inflammatory cytokines such as tumor necrosis factor α (TNF-α), interleukin-4 (IL-4), and IL-5, leading to an **inflammatory infiltrate** and perpetuation of longer-lived lesions.
- Angioedema is formed by a similar extravasation of fluid, not superficially in the skin but in the deeper dermal and subdermal sites.

Clinical manifestations

- Urticaria:
  - pruritic, edematous, erythematous, blanching papules that are round or oval in shape, have pale raised centers (wheals), are of several millimeters to a few centimeters in size, and are transient, lasting minutes to days
  - Loss of sleep, fatigue, and emotional discomfort.

Clinical manifestations

- **Angioedema**
  - brawny, nonpitting edema, typically with ill-defined margins and without erythema.
  - + sense of burning, pressure, or aching but not pruritus,
  - distinguished from other edematous states by often involving the lips, tongue, eyelids, hands, feet, or genitalia
  - rarely occurring in dependent areas of the body
  - symptoms vary from minor discomfort to an intense sense of pressure and may lead to other symptoms, such as severe shortness of breath.

Diagnosis

- **General:** CBC , ESR, urine and blood sugar, liver and renal function tests
- **Skin test:** commonly used in patient with chronic urticaria
- **Exclude certain disease** commonly associated with chronic urticaria as:
  - chronic suppurative infection especially sinus infection,
  - Infections with *Helicobacter pilory*
  - UTI,
  - hyperthyroidism,
  - *Diabetus Mellitus.,*
  - intestinal warms,
  - malignancy,
  - lymphoma,
  - pregnancy and
  - chronic exposure to external allergen (penicillin from cow milk).

Diagnosis

- Identifying special types of urticaria:
  - Elicit dermographism
  - Cold provocation and threshold test (Cold urticaria)
  - Pressure test (pressure urticaria)
  - Heat provocation and threshold test (Heat urticaria)
  - UV and visible light of different wave lengths (Solar urticaria)
  - Wet cloths at body temperature (Aquagenic urticaria)
  - Exercise and hot bath provocation (Cholinergic urticaria)
  - Prick/patch tes (Contact urticaria)
  - Exercise test (Exercise-induced anaphylaxis/urticaria)

Angioedema Classification

- **Allergic** (IgE mediated)
- **Non-allergic** (non IgE)
  - Hereditary angioedema (HAE)
  - Acquired (ACE inhibitors, COX inhibitors (pseudoalergic mechanism)
  - Physical
- **Idiopathic**

Treatment of Urticaria and Acute Episodes of Angioedema

- Non-sedating antihistamines (e.g. fexofenadine, desloratadine, cetirizine, loratidine)
- Diphenhydramine 50 mg (for more severe attacks)
- Prednisone 50 mg x 2 doses and stop without any taper
- Epinephrine – if rapidly advancing (EpiPen)
- H2 antihistamines and leukotriene modifiers can be added
- Rarely, corticosteroid sparing agents such as cyclosporine may be tried